

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 29619	FOR FURTHER ACTION		See item 4 below
International application No. PCT/IL2004/000279	International filing date (day/month/year) 25 March 2004 (25.03.2004)	Priority date (day/month/year) 27 March 2003 (27.03.2003)	
International Patent Classification (IPC) or national classification and IPC <sup>7</sup> A61K 31/4402			
Applicant APPELBAUM, Jerachmiel			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis. 1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I Basis of the report
<input type="checkbox"/>	Box No. II Priority
<input type="checkbox"/>	Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI Certain documents cited
<input type="checkbox"/>	Box No. VII Certain defects in the international application
<input type="checkbox"/>	Box No. VIII Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

Date of issuance of this report 04 November 2005 (04.11.2005)
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The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Authorized officer  Simin Baharlou  Telephone No. +41 22 338 71 30
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**PATENT COOPERATION TREATY**

From the  
**INTERNATIONAL SEARCHING AUTHORITY**

To:  
JERACHMIEL (YORI) APPELBAUM  
7 BIN ROGEL ST.  
JERUSALEM, ISRAEL 93543

REC'D 13 OCT 2005

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PCT

**PCT**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year)

**19 OCT 2005**

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/IL04/00279	25 March 2004 (25.03.2004)	27 March 2003 (27.03.2003)
International Patent Classification (IPC) or both national classification and IPC		
IPC(7): A61K 31/4402 and US Cl.: 514/332		
Applicant		
APPELBAUM, JERACHMIEL		

1. This opinion contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the opinion
<input type="checkbox"/>	Box No. II	Priority
<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application

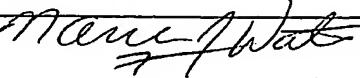
2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Phyllis G. Spivack Telephone No. 703-308-1235	
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/IL04/00279

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
 This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
 a sequence listing  
 table(s) related to the sequence listing
  - b. format of material  
 in written format  
 in computer readable form
  - c. time of filing/furnishing  
 contained in international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/IL04/00279

Box No. V Reasoned statement under Rule 43 *bis*,1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>2,3,23-30,32 and 33</u>	YES
	Claims <u>1,4-22 and 31</u>	NO
Inventive step (IS)	Claims <u>23,26-30,32 and 33</u>	YES
	Claims <u>1-22 and 31</u>	NO
Industrial applicability (IA)	Claims <u>1-33</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 2, 3, 23-30, 32 and 33 meet the criteria of PCT Article 33(2) as the prior art fails to teach each limitation of the claimed subject matter.

Claims 1, 4-22 and 31 fail to meet the criteria of PCT Article 33(2) as Ferdinand teaches compositions comprising TPEN and a pharmaceutically acceptable carrier, for inhibiting metalloprotease activity, treating ischemia-reperfusion injury, preventing the accumulation of nitric oxide and inhibiting the activity of a zinc-dependent enzyme.

Claims 1-22 and 31 fail to meet the criteria of PCT Article 33(3) as lacking an inventive step over Ferdinand. The determination of an optimal concentration of the active agent is a parameter well within the purview of those skilled in the art.

Claims 23, 26-30, 32 and 33 meet the criteria of PCT Article 33(3) as having an inventive step over the prior art.

Claims 1-33 meet the criteria of PCT Article 33(4) as they are directed to methods of treating a pathological condition influenced by MMP, and compositions, particularly comprising TPEN, therefor.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/IL04/00279

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 31/4402  
US CL : 514/332

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/332

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Ferdinandy et al., "Role of Nitric Oxide and TPEN, A Potent Metal Chelator, in Ischemic and Reperfused rat isolated hearts", Clinical and Experimental Pharmacology and Physiology, vol. 24, pp. 496-502 (1998), see entire document.	1, 4-22, 31
Y		2, 3
A		23, 24, 26-30, 33

Further documents are listed in the continuation of Box C.

See patent family annex.

• Special categories of cited documents:		
"A" document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

Date of mailing of the international search report

11 OCT 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (703) 305-3230

Authorized officer

Phyllis G. Spivack

Telephone No. 571-272-0585

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
PCT/IL04/00279

X	Ferdinandy et al., "Role of Nitric Oxide and TPEN, A Potent Metal Chelator, in Ischemic and Reperfused rat isolated hearts", Clinical and Experimental Pharmacology and Physiology, vol. 24, pp. 496-502 (1998), see entire document.	1, 4-22, 31
Y		2, 3
A		23, 24, 26-30, 33